

# Antioxidant status of Nigerians with diabetic disorders

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## Abstract

During the past few years, identification of many molecules that participate in cellular processes has contributed to the information on pathogenesis in many non-communicable diseases. The present study was undertaken to evaluate total antioxidant status (TAS) as a factor in the pathogenesis of diabetes mellitus. The study included 88 diabetic patients and 30 apparently healthy non-diabetic controls. On the basis of biochemical attributes, the different types of diabetics in the study groups were gestational diabetes mellitus GDM (22%), insulin dependent diabetes mellitus IDDM (23%), and non-insulin dependent diabetes mellitus NIDDM (55%). Blood glucose levels and plasma total antioxidant status were determined using standard methods. Plasma total antioxidant status levels were significantly lower in the diabetic groups than in controls ( $p < 0.05$ ). This finding was independent of the type of diabetes. On comparative basis, the lowest value of TAS was predominantly found amongst the IDDM. In this study, plasma TAS levels are markedly reduced in patients with all types of diabetes and hence an indication of the involvement of reactive oxygen species in the pathogenesis of diabetes and can be used as a prognostic marker in diabetic patients.

## Keywords

Diabetic Disorders, Antioxidant Status, Pathogenesis, Oxidative Stress

## 1. Introduction

Imbalance between production of oxygen free radicals (OFRs) and antioxidant defense can result in an oxidative stress, which leads to a variety of biochemical and physiological changes, often resulting in metabolic impairment and cell death [1]. Antioxidants are compounds with chemical affinity for free radicals [2]. They exist in abundance and bond with free radicals before they can cause damage. Antioxidants are of five classes: enzymes such as catalases, peroxidases and superoxide dismutase (SOD); peptides such as glutathione (GSH); phenolic compounds like vitamin E and plant flavonoids; nitrogen compounds, which includes various amino acids and carotenoids, most notably beta-carotene [3]. There is evidence in *in vitro* studies that cells deficient in GSH are

particularly sensitive to inflammatory cytokine (tumour necrosis factor alpha) [4].

Oxidative stress has emerged in recent years as a suspected component in the pathogenesis of diabetic disorders. It is suspected that even in the earliest stages of diabetic disorders, a deleterious reductive-oxidative (redox) imbalance may occur. The possible result is the uncontrolled presence of oxygen-containing molecules which could cause damage to cell membranes, proteins and nucleic acids, and alterations in the intra- and inter-cellular environments. OFRs have been implicated as a casual or contributing factor in many pathologic processes and have been suggested to cause peroxidation of membrane phospholipids, which can result in an increase in membrane fluidity, increasing permeability and loss of membrane integrity [5],[6]. The objective of this paper is to determine the pattern of plasma total antioxidant status (TAS) in the

different mechanisms underlying diabetic disorders.

## 2. Subjects and Methods

### 2.1. Subjects

Patients diagnosed clinically and biochemically as suffering from diabetes mellitus who attended the Medical Clinics of the University of Maiduguri Teaching Hospital, Northeastern Nigeria, were recruited into the study prospectively and consecutively. A total of 88 patients who had diabetes for a minimum of one year and without complications were enlisted into the study after screening about 150 suspects. The diabetic patients were classified as earlier described [7]. Patients with signs and symptoms of diabetes mellitus who did not conclude the blood glucose test following an overnight fast, and after 2 hour for postprandial blood glucose were excluded. 30 apparently healthy age and sex-matched control subjects who had no signs or symptoms of diabetes mellitus were enlisted into the study.

### 2.2. Methods

After informed consent and pre-test counselling in each case, 10ml of blood was collected aseptically by venesection, and appropriate volume dispensed into sodium fluoride and heparinized containers for blood glucose and TAS tests respectively. Blood glucose level was determined after enzymatic oxidation in the presence of glucose oxidase, the hydrogen peroxide formed reacts under catalysis of peroxidase with phenol and 4-aminophenazone to form a red-violet quinoamine derivative. The intensity of the colouration is proportional to the concentration of glucose in the blood sample, and was determined colorimetrically (Randox Laboratories, UK).

Plasma total antioxidant status (TAS) was determined using a commercial kit (Randox Laboratories, UK) based on a standard method [8]. In this test, ABTS (2, 2-Azino-di-(3-ethylbenthiazoline sulphonate) when incubated with a peroxidase (metmyoglobin) and hydrogen peroxide ( $H_2O_2$ ) produced the radical cation  $ABTS^{R4}$ . This has a relatively stable blue-green colour which was measured at 600nm. Antioxidants when added to a sample, caused suppression of this colour production to a degree which is proportional to their concentration.

Data were analyzed and Student's t-test was used to compare variables. Significance in the difference between results was inferred at  $p < 0.05$  [9]. Results were presented using appropriate models.

## 3. Results

Table I shows the age and sex distribution of the apparently healthy controls and the diabetic patients. The controls consisted of 19 males and 11 females. There were a total of 88 diabetic patients distributed as follows: GDM 19, IDDM 20 and NIDDM 49. Diabetic diseases occurred

mainly within the 20 – 59 years age range. More females (46) had diabetic diseases than males (42).

**Table 1.** Age and sex distribution of the controls and different diabetic

Age Group (yrs)	SUBJECTS							
	Controls (n=30)		GDM (n=19)		IDDM (n=20)		NIDDM (n=49)	
	M	F	M	F	M	F	M	F
0 - 19	-	-	-	-	-	-	-	-
20 - 39	16	11	-	15	1	1	8	12
40 - 59	3	-	-	4	8	2	17	8
60 - 79	-	-	-	-	3	3	4	-
> 80	-	-	-	-	1	1	-	-
<b>Total</b>	<b>19</b>	<b>11</b>	<b>0</b>	<b>19</b>	<b>13</b>	<b>7</b>	<b>29</b>	<b>20</b>
<b>Grand Total</b>	<b>30</b>				<b>88</b>			

GDM - Gestational diabetes mellitus, IDDM - Insulin dependent diabetes mellitus, NIDDM - Non-insulin dependent diabetes mellitus

Table 2 shows the plasma total antioxidant status (TAS) of the apparently healthy controls and groups of diabetic patients. The control group had TAS range of 1.38 – 1.80 mmol/L and group mean of  $1.6 \pm 0.2$  mmol/L. The difference in TAS results between the controls and IDDM patients who had mean TAS of  $0.7 \pm 0.4$  mmol/L and NIDDM patients who had  $0.7 \pm 0.3$  mmol/L was statistically significant ( $p < 0.05$ ). The patients with gestational diabetes mellitus had mean TAS of  $1.0 \pm 0.5$  mmol/L, with the difference statistically significant when compared with the controls ( $p < 0.05$ ). The GDM group however recorded the lowest single TAS value among the lot.

**Table 2.** Plasma total antioxidant status levels for the controls and different diabetic biochemical groups.

Group	TAS Values (mmol/L) Range	Mean $\pm$ SD	P Value
Controls (n=30)	1.38 - 1.80	$1.6 \pm 0.2$	-
GDM (n=19)	0.16 - 1.30	$1.0 \pm 0.5$	$< 0.05$
IDDM (n=20)	0.44 - 1.10	$0.7 \pm 0.4$	$< 0.05$
NIDDM (n=49)	0.48 - 1.40	$0.7 \pm 0.3$	$< 0.05$

GDM - Gestational diabetes mellitus, IDDM - Insulin dependent diabetes mellitus, NIDDM - Non-insulin dependent diabetes mellitus

## 4. Discussion

The present study clearly showed that plasma total antioxidant status (TAS) was significantly lower in all the

three groups of diabetic patients than non-diabetic controls ( $p < 0.05$ ). It is believed that the mechanism causing low levels of TAS in diabetic groups are related. This could be as a result of oxidative stress that is greatly increased in diabetes due to prolonged exposure to hyperglycaemia which leads to impaired generation of naturally occurring antioxidants [10]. Prolonged exposure to elevated levels of glucose is reported [11] to increase intracellular sorbitol and fructose content due to an aldose reductase and sorbitol dehydrogenase activity. In the reaction, oxidation of sorbitol to fructose is reportedly coupled to reduction of  $\text{NADP}^+$  to NADPH. Thus an increase in  $\text{NAD}^+/\text{NADH}$  ratio is linked to  $\text{O}_2$  formation via the reduction of prostaglandin  $\text{H}_2$  ( $\text{PGH}_2$ ) that uses NADH or NADPH as a reducing co-substrate. The replenishing mechanisms for the natural antioxidants are thus hindered.

Oxidative stress is a factor in many human diseases, as either cause or effect [12], and is an important step in carcinogenesis [13]. Antioxidants is believed to prevent many types of disease [14]. Antioxidants, in particular vitamin C, have been suggested to decrease oxidative DNA damage [15]. DNA damage may be associated with type 2 diabetes mellitus (T2DM) and its complications are mainly through oxidative stress [16]. Assays for antioxidant protection against oxidative damage generally depend on measurements of decreases in a marker of oxidation.

Low levels of free radicals are necessary for a number of important physiological functions including the inflammatory response, cell division and white blood cell action against bacterial infection [2].

## 5. Conclusion

It is important that a system of checks and balances is maintained between antioxidants and free radicals and their compounds, where the balance is weighed on the side of antioxidants. We believe this will be beneficial to diabetics.

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